Original Research Article

Thyroid hormone regulation in acute myocardial infarction patients

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Abstract

Aim: The aim of the present study was to evaluate changes in Free thyroid levels in patient of STEMI with cardiac markers Trop I and CKMB. **Material and Methods:** 100 Patients of STEMI were included. The diagnosis of STEMI based on the history of prolonged chest pain (> 30 min) was confirmed by ECG changes and with the help of biochemical markers like CK-MB, Troponin I and AST. 30 healthy subjects between 45- 70 years were taken as Control group.**Results:** The FT3 levels were on the lower side in patients of STEMI with cardiac markers on higher side, and the decrease was statistically significant. P<0.01. There was no significant difference in the serum concentration of FT_4 and TSH found between controls and cases. **Conclusion:** This study is conclusive, that there was decrease in mean serum FT_3 levels in patient of STEMI without significant changes in FT_4 and TSH as compared to controls. This downregulation of FT_3 was transient in patient of STEMI without complication and returns to normal or near to normal by the 7^{th} day but patient with sever AMI with complication and marked increase in CK-MB, Troponin I, the FT_3 value still not came to normal levels**.**

Keywords: acute myocardial infarction,biochemical,markers

Introduction

Ischemic heart disease is already the leading cause of mortality in India[1] and the magnitude of impact of this disease is expected to grow over the next two decades[2]. It is projected that ischemic heart disease will result in two and one-half million Indian deaths by 2020[3]. Acute coronary syndrome (ACS), including both ST-elevation myocardial infarction (STEMI) and non-ST elevation STEMI (NSTE-STEMI), is an important manifestation of ischemic heart disease.

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Acute coronary syndrome is a set of signs and symptoms related to the heart. STEMI is compatible with a diagnosis of acute myocardialinfarction, but it is not characteristic of the diagnosis.

The sub-types of acute coronary syndrome include unstable angina and two forms of myocardial infarction in which heart muscle is damaged. These types are named according to the appearance of the electrocardiogram (ECG/EKG) as non-ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI)[4]. There can be some variation as to which forms of MI is classified under acute coronary syndrome.

Abnormalities in thyroid homeostasis also occur in variety of non- thyroidal illnesses. Changes in thyroid hormone metabolism in critical illnesses appear to reflect a continuity which relates primarily to the severity of the disorders[5]. The prevalence of one or more abnormalities of thyroid function tests in

patients with non thyroidal medical illnesses has been reported from 40% to 70%[6].The condition is reported in starvation[7], sepsis[8], surgery[9], myocardial infarction[10], CABG surgery[11], bone marrow transplantation[12] and in fact probably any severe illness.Serum thyroid hormone levels have been described in several systemic non-thyroidal illnesses, among them one of the causes was acute heart diseases. The changes observed in these NTIS have been classified as "Euthyroid sick syndrome". Euthyroid sick syndrome consisting of low total T3 and/or free T3, increased reverse T3 (rT3) and normal TSH, T4 and free T4 levels. These findings are seen in acute myocardial infarction, affecting the prognosis[13]. These changes in thyroid function was thought to be associated with the mechanism involved in maintaining energy in face of altered systemic homeostasis caused by the acute ischemic event[14] or directly related to inflammatory cytokines, acting as an inflammatory marker or both [15]. Acute myocardial infarction may induce profound change in number of neuro-endocrine systems. The changes within the hypothalamic-pituitary-thyroid (HPT) axis also occur in illness and typically associated with low levels of total tri-iodothyronine (T_3), and this gives rise to term "**low T_3 syndrome".** Sick patients with low serum T_3 were often regarded as being clinically euthyroid and as consequences, the alternative term**"Euthyroid sick syndrome"** was widely used in past. **"Non-thyroidal illness syndrome" (NTIS)** is now more commonly used to describe the typical changes in thyroid related hormone concentrations which can arise in the serum following any acute or chronic illness, which was not caused by an intrinsic abnormality in thyroid function[16]. In recent decades it has become increasingly apparent that acute and chronic cardiovascular diseases may alter thyroid hormone metabolism and contributes to cardiovascular impairment. This syndrome has been found in acute myocardial infarction (AMI) and as a rapidly emerging phenomenon during open heart surgery. The more profound change in thyroid hormone pattern, the poorer is the prognosis[17]. In this study, I investigated potential changes occur in thyroid hormone levels in patient presenting to intensive cardiac care unit with acute myocardial infarction and those were previously euthyroid without having any disorder related to the thyroid hormone function.I also compared ST-segment elevated acute myocardial infarction (STEMI) with respect to degree of change in levels of biochemical marker of cardiac injury like, Createnine kinase MB isoenzymes (CK-MB), Trop1onin I and Aspartate amino- transferase (AST) and their relation with thyroid hormone changes in patients of STEMI.

Material and Method

The present study was conducted in Department of biochemistry during December 2018 to May 2019. 100 patients with first episode of acute coronary syndrome, who were admitted in the intensive cardiac care unit 1to 6 hours after onset of pain between the age group of 45 to 70 years, were included in study.The diagnosis of STEMI based on the history of prolonged chest pain (> 30 min) was confirmed by ECG changes and with the help of biochemical markers like CK-MB, Troponin I and AST.Age and sex matched apparently normal healthy controls were taken.Blood sample were collected in plain bulb atthe time of admission within 6hr and at 24-36 hr, 72hr and 7 days after onset of symptoms, for the serial estimation of :-Free tri-iodothyronine (FT_3) Free thyroxine (FT_4) Thyroid stimulating hormone (TSH) And estimation of cardiac biomarkers like CK-MB,Troponin I and AST Were done on sample collected at 24 to 36hr .A standard 12-lead electrocardiogram was obtained by the regular procedure.

Definition of study subjects

Group I : Control subjects

- 30 healthy subjects between 45- 70 years were taken Group II : Patients with acute coronarysyndrome
- 100 patients of acute coronary syndrome admitted in I.C.C.U between the age group of 45-70 years were taken.
- ST segment elevation Acute Myocardial Infarction (STEMI)

Inclusion criteria

- Patients presenting with first episode of acute coronary syndrome with or without complication. (Arrhythmias, Cardiac arrest)
- Patients without any past history of thyroid related disease and/or abnormality.

All details about the study were explained to the subject and informed consent was taken. Blood sample were collected from cubital vein by explaining the procedure to the subjects. Approximately 5 ml of blood was collected in a clean, dry, sterile plain bulb.Blood sample allowed to coagulate for 2-3 hr and serum was separated by centrifugation at 3000 rpm for 10 minutes.

Results

100 cases of STEMI were investigated, Serum was analysed for FT3, FT4, TSH. CPKMB, Trop I and AST. Table 1 showing the mean values of FT_3, FT_4, and TSH with standard deviation.

Serial estimation of FT_3, FT_4, and TSH done at < 6hr, 24 to 36 hr,72 hr and 7 days done in the cases. A statistical difference evaluated by t test and two tailed p value < 0.05 was accepted as significant statistical analysis.

FT_3 P value of control (e) vs a **p >0.05** (NS), **NS**= not significant***control (e) vs b and c **p < 0.00001**(very significant), *control (e) vs d **p< 0.05** (significant) FT_4 and TSH p value of control (e) vs a b c d is (NS) i e > **0.05**,FT_3 within cases ***p< **0.00001**, **p < **0.001**

Table 1: Mean values of FT_3, FT_4, and TSH with standard deviation

Parameter	Cases of STEMI (n=100)				Control(n=100)	P-value
	<6hr(a)	24 –36 hr(b)	72 hr (c)	7day(d)	(e)	
FT_3 (pg/ml)	2.59± 0.79	1.36±0.68***	1.80±0.67**	2.24± 0.76*	2.51± 0.70**	a vs b***, a vs c ***, a vs d**
FT_4 (ng/ml)	1.26± 0.32	1.18± 0.30	1.22± 0.34	1.27± 0.32	1.21± 0.26	NS
TSH(µlU/ml)	3.65± 1.70	3.68± 1.69	3.77± 1.76	3.94± 1.79	3.24± 1.53	NS

Table 2:FT_3, FT_4, TSH in Subgroup STEMI

Diagnosis	F T_3 (pg/ml)	F T_4(ng/ml)	TSH(µlU/ml)
<6hr			
STEMI	2.52 ± 0.79	1.23±0.32	3.94±1.82
P value	NS	NS	0.03
24 – 36 hr			
STEMI	1.29 ± 0.69	1.16±0.30	3.95±1.81
P value	NS	NS	0.03
72 hr			
STEMI	1.74±0.68	1.20±0.35	4.07±1.88
P value	NS	NS	0.02
7 day			
STEMI	2.18±0.81	1.23±0.31	4.25±1.90
P value	NS	NS	0.01

Table 2 the FT_3,FT_4 and TSH in two subgroups STEMI. There was no significant difference in the FT_3 and FT_4 p value >0.05 (NS) but p value < 0.05 in TSH of STEMI and NSTEMI. Table 2

Table 3:Correlation of FT_3 and CK-MB, Troponin I

Parameter	CK-MB	Troponin I
FT_3 (24- 36hr)	**-0.376 (p < 0.001)**	**-0.300 (P=0.002)**

There was significant negative correlation found between 24-36 hr FT3 with CK-MB, Troponin I and AST with P value of less than 0.05 **(p <0.001, p = 0.002, p = 0.005 respectively)**.

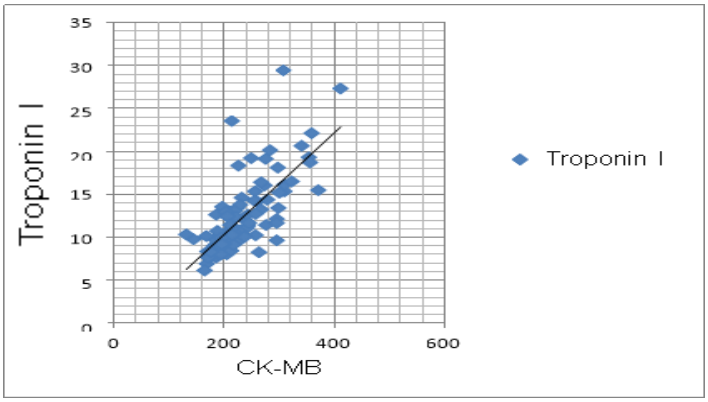

Fig 1:Correlation of Troponin I and CK-MB of cases

Discussion

Acute coronary syndromes are serious condition that may affect thyroid gland homeostasis, with the implication in terms of morbidity and mortality[18]. This study was used to investigate whether thyroid hormone levels would present a distinct behavior in the STEMI was associated with more complications like arrhythmia, cardiac arrest and poor prognosis, showing unique pathophysiological features that determines the thrombus and requiring reperfusion strategies, either by thrombolytics or mechanical recanalization.In my study, on analysis of hormonal behaviour in patients admitted for coronary heart disease showed decrease mean serum free T_3 levels as compared to the control group (p value < 0.00001), while the other hormones free T_4 and TSH remained unchanged.These findings of above study shows that, there is decreased serum FT_3 values of patient as compared to control. Also I got the significant negative correlation between the specific markers of severity of cardiac injury CK-MB (p< 0.001) and values of FT_3.Yet in another 11 months prospective study in three groups of patients admitted to emergency department, 95 patients with chest pain and proven AMI, 26 patients with chest pain and no AMI, and 114 patients who served controls with no evidence of any major disease, sixteen patients (16.8%) with AMI died within the study period, Troponin T and CK-MB levels were significantly high in nonsurvivors when compared with survivors. Survivors in the AMI group had higher TT_3, TT_4 and lower FT_3 and FT_4 levels than controls. In AMI group, the non survivors had lower TT_3 and FT_3 levels than the survivors. These findings of above study supports the finding of my study that there was a decrease in the FT_3 levels in patient of AMI and this decrease in the levels of $FT_3$was proportional to the severity of AMI. This relation of FT_3 in patient of AMI may be appearing to be independent prognostic factor in patients with AMI[21].The probable mechanisms for the transient decrease in serum FT_3 levels were multifactorial and can be attributed to:

1. Decreased hepatic conversion of $T_4$to T_3, espesially in advanced heart failure, as a result of decreased in activity of 5' monodeiodinase. This decreased activity also reduces peripheral conversion of $T_4$to T_3,diverting it to inactive reverse T_3pathway
2. An expanded blood volume ofdistribution
3. A short half life T_3 [19,20]

If these seemingly disadvantageous effects of decreased production of biologically active T_3 were important, patients with more marked hormone derangement would have a worse prognosis regarding heart function and survival. I have reported significant positive correlation between degree of thyroid hormone level depression and severity of AMI[21].

Conclusion

In the present study, I serially estimated thyroid hormone FT_3, FT_4 and TSH in patient with Acute myocardial infarction and compared them with healthy age, sex matched apparently normal control group. Also, I correlated the relation of change in thyroid hormone with markers of cardiac injury CK-MB, Troponin I .I studied 100 patients with STEMI, out of which 35% patient having "Euthyroid Sick Syndrome", a condition characterised by decreased serum T_3 and/or free T_3, increased reverse T_3, plus normal serum TSH, T_4 and free T_4. From my present study I came to conclusion that there was decrease in mean serum FT_3 levels in patient of STEMI without significant changes in FT_4 and TSH as compared to controls. This downregulation of FT_3 was transient in patient of STEMI without complication and returns to normal or near to normal by the 7^{th}day but patient with sever AMI with complication and marked increase in CK-MB, Troponin I, the FT_3 value still not came to normal levels.There was no significant difference found in changes in thyroid hormone profile in STEMI and NSTEMI group. Also I found significant negative correlation between the markers of cardiac injury CK-MB, Troponin I and the degree of decrease in free T_3 levels in these patients.Thus, I concluded that, the thyroid hormone system was rapidly downregulated in acute coronary syndrome, which may be beneficial during acute ischaemia. The degree of free T_3 decrease was proportional to the severity of cardiac damage and may have a possible prognostic value. Thus, free T_3 serum levels may contribute to the elaboration of an STEMI severity index.

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